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Paranasal Mucormycosis in immunocompromised host (Early diagnosis is the key)

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ABSTRACT

Mucormycosis is an emergent life threatening fungal infection that has potential risk of dissemination with significant morbidity and mortality rate particularly among patient with altered immune status. Here, we report a case with hematologic malignancy, who admitted with febrile neutropenia and developed left sided facial swelling on day five on his admission. Early nasal endoscopy lead to early diagnosis of mucormycosis with limited invasion. Treatment with Liposomal amphotericin B for 3month duration was administered intravenously with multiple nasal-endoscopic surgical debridement which result in good recovery without significant morbidity.

Keywords: Mucormycosis; Zygomycetes; Acute lymphoblastic leukemia; Endoscopic debridement

1. INTRODUCTION

Mucormycosis is a fulminant invasive saprophytic fungal infection, which is found frequently among immunocompromised patients (Patterson, 2005; Fisher et al., 2018). The prevalence of mucormycosis cases projected to rise over the past two decade as a result of increased number of cancer patient, prolonged use of intravenous catheters, excessive use of antifungal prophylaxis and bandages (Kontoyiannis et al., 2000). The most common predisposing factors for developing such fungal infections are the presence of an uncontrolled diabetes mellitus, immunocompromised patients with underlying conditions such as malignancies, steroid therapy, IV drug abuse, chronic renal failure, burns and sustained skin trauma (Roden et al., 2005). Here we are reportinga case of mucormycosis and discussing the clinical course therapeuticand diagnostic issues.

2. CASE

This study was conducted during 2019-2020. 40 year old male ex-smoker not known to be diabetic known case of hypertension, newly diagnosed acute lymphoblastic leukemia (ALL) admitted to hospital as a case of pancytopenia and febrile neutropenia. He had history of subjective fever, dry cough and gradually progressing shortness of breathfor 1 month duration. CXR and HRCT reveled right side pleural effusion with bilateral scattered speculated

pulmonary nodules likely represented underlying leukemic infiltration and the possibility of community acquired pneumonia was considered. Pigtail insertion was donepleural effusion analysis was suggestive of exudative effusion.He started empirically on Tazocin and started on the Dana Farber consortium protocol (DFCP) for (ALL). Bronchoscope donerevealed normal study with positive bronchial alveolar lavagePCR ofMycoplasma pneumonia, Levofloxacin was added.

Five days later patient developed diffuse tender swelling over left maxillary and peri-orbital area with purulent nasal discharge. Paranasal sinus CT scan showed total opacification of the left nasal cavity with minimal widening left ethmoid air cells opacification and mucosal thickening of the left maxillary sinus with left osteomeatal complex obliteration. Endoscopic endonasal examination showed edematous mucosa and congestion with no evidence of necrosis. Biopsy taken during examination demonstrated fungal organisms which were thick walled had non septate hyphae compatible with Mucormycosis (Figure 1). Urgent endoscopic endonasal debridements of the necrotic tissues are done with complete removal of middle and inferior turbinate. He started on double anti-fungal therapywith liposomal amphotericin B and micafungin.Vancomycin, levofloxacin and (DFCP) protocol discontinued Granulocyte colony stimulating factor (G-CSF) given. Micafungin discontinued after 7 days of treatment as symptoms improved and left maxillary and peri-orbital swelling regressed. Ophthalmic examination was unremarkable.

Pan CT reported hepato-splenic abscess was aspirated and culture showed carbapenem resistance pseudomonas aeruginosa (CRP) growth, which complicated by bacteremia. Colistin added to meropenem for CRP coverage. Patient developed purulent paranasal secretions culture taken and revealed (CRP) growth. Liver enzyme ALT 210g/dl, AST 293g/dl, ALP 119 g/dl, GGT 561 g/dl and serum total bilirubin 3.3 g/dl started to be increased, an ultrasound of hepatobiliary system found a calculus cholecystitis, cholecystostomy aspirated fluid grew CRP. Micafungin was resumed by day 25 of initiation of liposomal amphotericin B in view of persistent mucormycosis growth in the follow up endoscopic endonasal biopsies.

Febrile neutropenia resolved by day 34 of initiation antifungal therapy. The follow up endoscopic endonasal examination showed crustation all over the nasal cavity with fresh granulomatous healthy tissue with no evidence of necrotic tissue. Biopsy taken has showed no evidence of mucormycosis. (DFCP) chemotherapy protocol resumed. Follow up paranasal CT showed stable appearance of nasal sinuses with chronic inflammatory changes. Micafungin was discontinued and patient was continued on liposomal amphotericin B for total 3 month duration. Meropenem and colistin discontinued in view of negative repeated blood culture and regression of splenic lesion in the follow up CT abdomen after 6 weeks apart from previous of the CT images. Patient improved clinically and discharged on posaconazole as secondary fungal prophylaxis.

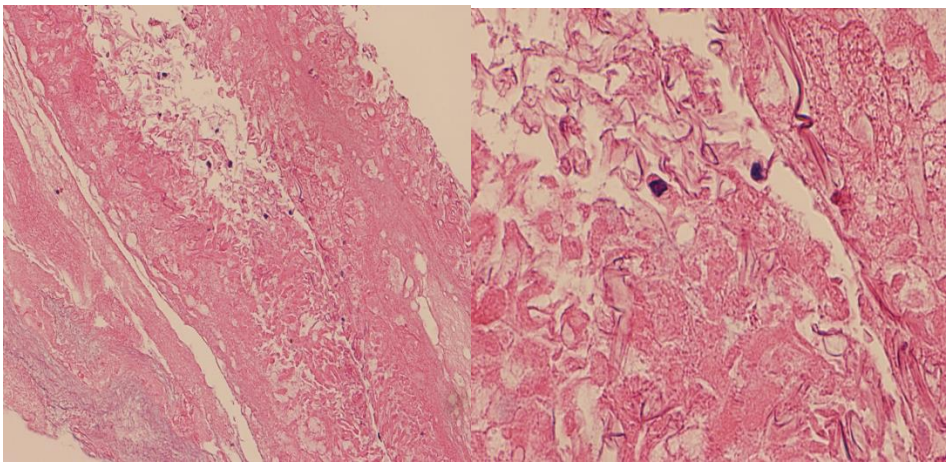

Figure 1 Fungal organisms with thick wall had non septate hyphae

3. DISCUSSION

Mucormycosis is a critical rarity fungal infection with high mortality rate caused by fungi genera affiliated with the Mucorales species (Viterbo et al., 2011). In our presenting case the patient had immune altered status secondary to underlying hematological malignancy with possible risk less than 1% incidence of mucormycosis. Abdollahi et al., (2016) had persistent fever followed by tender swelling over the left side of his face which represent the most common early reported symptom of mucormycosisin addition to nasal ulceration or necrosis, periorbital swelling and impaired vision (Del Valle et al., 1996). We have established our work up diagnosis by computed tomography scan that reveled total opacification of the left nasal cavity with minimal widening with left ethmoid air cells opacification and mucosal thickening of the left maxillary sinus with left osteomeatal complex obliteration. Paranasal sinuses are the most frequent anatomical site for mucormycosis (39%), followed by pulmonary (24%),

cutaneous (19%), cerebral (9%), gastro-intestinal (7%), other (6%) or disseminated (6%) (Roden et al., 2005). Nasal endoscopic examination and excisional biopsy was performed for our patient and histopathology result illustrated mucoidy material only with few neutrophils and focal infestation of non- septate thick walled fungal hyphae (highlighted on PASD stain) compatible with invasive mucormycosis.

The fundamental component of therapy in particular patient with mucormycosis is to address the underlying disease process and correct the neutropenia by administration of G-CSF that been shown to increase the fungicidal effect of the polymorphonuclear leukocytes and improve their other defensive function (Gaviria et al., 1999). Our next step was to performed early Nasal endoscopic debridement of the affected tissue combined with administration of Polytherapy of liposomal amphotericin B 5 to 10 mg / kg / day in addition to Micafungin 1 mg/kg/day among neutropenic patient have extremely positive impact on mucormycosis survival (Skiada et al., 2013; Ibrahim et al., 2008). Duration of anti-fungal therapy generally continued whenever the clinical signs and symptoms resolved with negative follow up biopsy of debrided tissue and regression of inflammatory process on serial radiological imaging (Chamilos et al., 2008a; Kontoyiannis and Lewis, 2011).

Adjunctive hyperbaric oxygen therapy utilized as therapeutic agent for mucormycosis since 1970s with minimal side effect Several studies demonstrate that hyperbaric oxygen has fungistatic activity potentiate the action of Amphotericin B and the major effect is enhancing affected tissue oxygenation (Goel et al., 2009). Using of hyperbaric oxygen as adjunct strategy in addition to surgical debridement and antifungal therapy it shows significant increasing in the survival rate among affected patient (Hendrickson and Olshaker, 1999; Tragiannidis and Groll, 2009). Delay in Mucormycosis diagnosis more than 5 days is strongly resulting in significant increase in the mortality rate reaching up to 50 % among the affected patient (Chamilos et al., 2008b; Katragkou et al., 2014). There were limited retrospective surveillance study done by Dönmez Çavdar et al., (2013) presenting promising result for early mucormycosis detection by Mucorales qPCR assay as a screening tool among immunocompromised patient.

In another retrospective study performed by Silveira et al., (2019) they suggested to proceed for nasal endoscopic examination with histopathological biopsy when appropriate for all immunocompromised and neutropenic patient with persistent fever after 48 hours of broad spectrum intravenous antibiotic lead to early detection of mucormycosis with limited in invasiveness of the disease at diagnosis and careful post-operative follow up resulted in better outcome by comparison with other study (Turner et al., 2013; Valera et al., 2011; Foshee et al., 2016; Payne et al., 2016; Cho et al., 2015; Gillespie and O'Malley, 2000). Early diagnosis was the most important factor for significant decrease in morbidity and good outcome in our patient.

4. CONCLUSION

Mucormycosis is a saprophytic fatal fungal infection with potential risk of invasion and dissemination. Controlling the underlying precipitating condition is the key role of management in such infection. Early diagnosis and treatment with broad-spectrum antifungal agent and extensive debridement of the affected tissue associated with good chance of treatment success and improve survival. There is a need for better consensus guidelines for optimum screening method for early diagnosis of mucormycosis in patient with hematological malignancy.

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Author Contributions

All authors provided data, wrote and contributed to the final manuscript.

Informed consent

Written consent was obtained from the patient.

Ethical approval

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Conflict of Interest

There are no conflicts of interest.

Data and materials availability

All data associated with this study are present in the paper.

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